PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
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PCT

Reply To:
WRITTEN OPINION
(PCT Rule 66)

DUE ON APR 28 2004

Date of mailing (day/month/year)	28.01.2004
Applicant's or agent's file reference 12863 ~~13022~~-2PCT	REPLY DUE within 3 month(s) from the above date of mailing

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/CA 03/00617	24.04.2003	24.04.2002

International Patent Classification (IPC) or both national classification and IPC
C12N5/06

Applicant
BIOGENTIS INC. et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III.	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 24.08.2004

Name and mailing address of the international preliminary examining authority:
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WRITTEN OPINION

International application No. PCT/CA 03/00617

I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-11 as originally filed

Claims, Numbers

1-26 as originally filed

Drawings, Sheets

1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

WRITTEN OPINION International application No. PCT/CA 03/00617

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1, 2, 5-7, 9-11, 13-16, 18-26
Inventive step (IS)	Claims	1-26
Industrial applicability (IA)	Claims	

2. Citations and explanations

see separate sheet

WRITTEN OPINION
SEPARATE SHEET

International application No. PCT/CA03/00617

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1 L'Heureux et al., *Faseb Journal*, 1998, 12, 47-57 (January 1998)

D2 US 6,133,030 A (General Hospital Corporation; Massachussets Institute of Technology) 17 October 2000

D3 WO 00/66036 A (Massachussets General Hospital) 9 November 2000

D1 describes a process for making artificial blood vessel constructs by wrapping sheets of vascular smooth muscle cells and fibroblasts aroung a tubular support; in this process, full contact between the cell sheets occurs. As far as the tissue construct of claim 1 is a blood vessel, as provided by the example of the application, it is not new over the vessel constructs of D1, the subject-matter of claims 18-26 therefore lacks novelty (Article 33(2) PCT).

D2 describes the co-cultivation of cells on micro-patterned supports. Part II of D2 specifically describes the contruction of artificial liver constructs with hepatocytes grown as continuous populations over desgnated parts of the support and fibroblasts grown on the remaining parts of the support, resulting in edge contcat between the two cell populations along the lines of the pattern. Part III compares this setting with co-cultures where cells are separated by removable polyme- annuli. While no examples are given, the use of other cell types is considered, including endothelial cells and smooth muscle cells (col. 2, point c). In view of this prior art, the subject-matter of claims 1, 2, 5-7, 9-11, 13-15 and 18-26 is not new (Article 33(2) PCT) and the additional subject-matter of claims 3, 4, 8 and 12 does not involve an inventive step over D2 (Article 33(3) PCT).

D3 describes a process for making three-dimensional vascularised organs by growing a branching pattern of vascular cells on a two-dimensional mold, applying a sheet of cells (in the example, hepatocytes) to the resulting vascular structure and eventually rolling the vascularised cell sheet into a three-dimensional cylinder; obviously, edge contact between the two cell population occurs along the lines of the pattern. In view of this prior art, the subject-matter of claims 1, 2, 5-7, 9-11, 16 and 18-24 is not new (Article 33(2) PCT) and the additional subject-matter of claims 3, 4, 12 and 17 does not involve an inventive step over D3 (Article 33(3) PCT).

None of the prior art documents describes or suggests a process of rolling a single tissue construct

comprising a population of vascular smooth muscle cells in one domain and a population of fibroblasts in another domain to produce a blood vessel construct, it is thus suggested to draft a new independent claim incorporating these features.

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description, nor is this document identified therein.